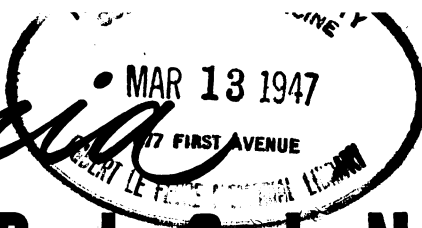


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Demerol Analgesia In Obstetrics*

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IT may sound strange to say that the medical profession is still in quest of a satisfactory and constantly applicable method of analgesia for the pain of childbirth in view of the dramatic relief offered by continuous caudal analgesia. After reading some of the enthusiastic reports on continuous caudal analgesia, one is likely to conclude that the suffering of parturition has been finally abolished. But it must be pointed out that this procedure is not universally applicable because of certain limitations. It is a highly technical procedure requiring special training and a great deal of practice, and adaptable to patients only in well staffed obstetrical institutions. It demands constant attendance and supervision by the obstetrician during the entire course of its administration.

Despite perfect technique and proper selection of patients, caudal analgesia fails to produce relief of pain in a certain percentage of cases and many patients refuse the procedure because of fear or prejudice. Most important, caudal analgesia carries a definite risk to the patient's life, even in the best of hands, as shown by occasional maternal complications and deaths due directly to the procedure. For these reasons other forms of obstetrical analgesia are still being sought, especially by physicians who do not find optimal conditions in their communities for routine use of caudal analgesia. The shortage of doctors and nurses during the present crisis, and the consequentially greater demand on their time by patients, has certainly curtailed their ability to remain with parturients during the entire course of caudal analgesia.

Doctors and nurses were in short supply in the Sonoma County Hospital, as elsewhere, during the past two years. Hence, a method of analgesia was sought that would produce the desired relief

from pain during labor and at the same time be safe for mother and child and be relatively easy to administer and supervise. After several agents had been tried, Demerol was chosen as the drug meeting such specifications.

From the number of reports in three years on the use of Demerol, alone or in combination with some other agent, it is evident that the drug has already assumed an important place in obstetrics. After a preliminary report by Roby and Schumann² of the Boston Lying-in Hospital, the latter¹ presented a thorough study of 1,000 labors conducted under Demerol-scopolamine analgesia, with an inhalant for actual delivery. In view of the satisfactory amnesia, absence of pulmonary complications, and freedom from depressant effects on the fetus, Schumann concluded that Demerol in conjunction with scopolamine is superior as an obstetrical analgesic to other analgesics in common use. In December, 1945, Carter⁵ reported a series of approximately 2,700 cases from three hospitals in Madison, Wisconsin, in which, after a small preliminary dose of a barbiturate, analgesia was obtained by Demerol-scopolamine, with delivery under nitrous oxide and oxygen. Carter considers that Demerol combined with scopolamine or some other agent is not surpassed by any drug or method now in use.

DEMEROL

Demerol, or ethyl 1-methyl-4-phenylpiperidine-4-carboxylate, is a synthetic agent exhibiting properties comparable to those of both morphine and atropine; the analgesic power is close to that of morphine and the spasmolytic action weaker than that of atropine. It differs from morphine in that it relaxes smooth muscle. The appealing property from an obstetric standpoint is the apparent absence of any significant depressant action on the patient. Uterine contractions are not slowed and the spasmolytic action on the

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cervix is evident by the rapid dilatation of that organ during labor. Demerol was reported to produce a slight elevation of the blood pressure, especially in toxemic patients, but Carter found little noticeable effect on pulse or blood pressure. The risk of addiction is negligible in the amounts employed obstetrically.

Adequate amnesia is not always produced by Demerol alone, as several investigators⁴ have found, but the addition of scopolamine or a barbiturate generally results in a high percentage of amnesia. Scopolamine is preferred, since there is practically complete freedom from the crises of pulmonary edema seen occasionally with barbiturates. Moreover, Schumann states that the psychic sedation obtained by Demerol through its analgesic effect provides a favorable background for the action of scopolamine, reducing excitement and enhancing amnesia. In most reports, the usual dosage of Demerol was 100 mg. administered intramuscularly when the patient became uncomfortable. Additional doses were injected at intervals thereafter. Less relief was provided by oral administration. Mild side-effects rather frequently follow intravenous administration of Demerol, but the rapid control of pain and increased amnesic effects procured through very slow intravenous administration offer definite advantages, particularly in multiparas. In the present study the intramuscular route was used exclusively.

MATERIAL

Demerol was administered to 300 women in labor at the Sonoma County Hospital between February 1, 1945, and April 1, 1946. These patients were unselected, except that the drug was not given to any patient with toxemia. So far as it is known, toxemia is the only contra-indication to the use of Demerol in obstetrics. A total of 307 infants was born to the 300 mothers, as follows:

| Type of Delivery | Number | Percentage |
|----------------------------|--------|------------|
| Spontaneous | 233 | 77.6 |
| Low forceps | 40 | 13.3 |
| Breech Extraction..... | 10 | 3.3 |
| Mid-forceps | 7 | 2.3 |
| Twins | 5 | 1.6 |
| Version and extraction.... | 4 | 1.3 |
| Triplets | 1 | 0.6 |

A control group of 300 similar patients was given nembutal, seconal, paraldehyde, dial and scopolamine in varying combinations and doses.

In addition to these 300 vaginal deliveries, there were 14 Caesarean Sections premedicated with Demerol. Because the problem of labor was not present in the majority of this group, it will be discussed in a separate section.

METHOD OF ADMINISTRATION

The following routine of administration was adopted: Demerol 100 mg. and scopolamine 0.48 mg. (1/150 grain) were given intramuscularly as soon as the patient in active labor began to complain, regardless of the degree of cervical dilatation. This combination was repeated in three hours, and Demerol alone given in 100 mg. doses

at three-hour intervals thereafter until the patient was ready for delivery. An attempt was made not to give Demerol or scopolamine within an hour of expected delivery as an additional precaution against possible fetal anoxia. As the study progressed, it was found that Demerol given within an hour of delivery produced no demonstrable depressant effect on the child, whereas the combination of Demerol and scopolamine given similarly resulted in several "slow" babies, that is, babies which required more than the routine measures of resuscitation. The more apprehensive patients were given 0.1 gm. of nembutal or seconal (1½ grains) by mouth at the same time the original dose of Demerol and scopolamine was administered. The barbiturate was not repeated thereafter during labor. This group of patients appeared better sedated than those receiving Demerol and scopolamine alone, and the infants showed no unusual depression. However, the number was too small to permit any valid conclusion.

Of the 300 patients, 250 required but *one dose* of Demerol for their entire labor; 40 patients were given *two doses*, 7 received *three doses*, and 3 had *four doses* or a total of 400 mg. In nearly all cases nitrous oxide and oxygen were used during the second stage of labor. Certain difficult deliveries necessitated continuous nitrous oxide and ether anesthesia. Most of the episiotomies and repairs were performed under pudendal block and local infiltration with 1 per cent Novocain solution.

EVALUATION OF ANALGESIA AND AMNESIA

In the great majority of patients, Demerol and scopolamine produced relief of pain and evidence of sedation within from 15 to 20 minutes after intramuscular administration. The patient usually relaxed, stopped crying and complaining, and fell into a light sleep, rousing somewhat during the pains. The analgesic effect lasted from two to six hours, averaging about three hours.

The patients were interviewed a day or two after delivery for their memory of labor. On the basis of the interview, they were divided arbitrarily into those having (1) complete analgesia and amnesia, (2) satisfactory analgesia, and (3) unsatisfactory analgesia. In the first group fell those having completely painless childbirth without the impingement on the patient's memory of pain or suffering following the administration of Demerol. In the satisfactory group were placed those who remembered isolated incidents during labor but whose suffering was markedly or completely relieved. This group also included patients who volunteered satisfaction with the method and those who referred other patients asking specifically for Demerol in their forthcoming deliveries. Patients with borderline analgesia were not placed in this group. The unsatisfactory group included those claiming no relief with Demerol, the ones who received medication too late in labor for effective action, and those who did not receive the drug according to plan.

Complete analgesia and amnesia was obtained in 126, or 42 per cent, of patients and satisfactory analgesia in an additional 182, or 44 per cent. This gave a combined total of 86 per cent with satisfactory analgesia. In the third group there were 42 patients, 14 per cent, who failed to obtain adequate relief or who did not receive the drugs soon enough or according to plan.

In contrast, only 48 per cent of the control patients obtained satisfactory sedation with the barbiturates, paraldehyde and scopolamine and 52 per cent had unsatisfactory analgesia. The uncorrected 86 per cent incidence of satisfactory sedation in the Demerol-scopolamine treated patients would undoubtedly have been higher had medication been administered earlier or according to plan in the remaining 14 per cent.

LENGTH OF LABOR

The most interesting observation in the majority of the Demerol patients was the rapid cervical dilation that occurred after medication. It was not at all unusual for a primiparous cervix to progress from a dilation of about 2 cm. to complete dilation in the space of from two and one-half to three hours after injection of Demerol.

In the group of 165 primiparas, the length of labor averaged 11.2 hours, as compared with 15.4 hours' labor in the control primiparas. In 135 multiparas, the duration of labor was, on the average, 7.0 hours. The duration of labor in the control multiparas was 9.2 hours. Hence, labor lasted 4.2 hours less in the primiparas and 2.2 hours less in the multiparas treated with Demerol, as contrasted with the control series, reductions of 27 and 24 per cent, respectively, in the duration of labor. Stated differently, about 85 per cent of Demerol-treated patients were in labor for less than four hours after administration of the drug. While it is obvious that a few relatively long or short labors might alter considerably the average figures in a comparatively small series of patients, the same conditions also held in the control series of 300 patients.

UNTOWARD EFFECTS

No untoward effects of any importance were observed. It is possible that these were avoided by not giving the drug intravenously. The following transitory side reactions were noted: Dryness of the mouth and throat in 82 per cent, nausea in 28 per cent, dizziness in 14 per cent, diaphoresis in 12 per cent, vomiting in 6 per cent, and excitement in 4 per cent of the subjects. By way of contrast, the manic state was observed in over 20 per cent of the control subjects given barbiturates and paraldehyde analgesia. There were no instances of edema of the uvula or glottis, as recently reported by Steinberg³ after Demerol-scopolamine analgesia and attributed in all probability to scopolamine. The absence of edema of the uvula in the present series may be due to the fact that minimal amounts of scopolamine were used. There was

no significant evidence of narcotic depressant action and most patients were completely oriented within three hours after delivery. Usually they were able to converse and answer questions during the period of sedation, but little memory of this was retained afterward.

RESULTS IN INFANTS

Schumann's method of classifying the infants according to their condition upon delivery was followed. *Group A* includes those who breathed spontaneously and required no treatment other than the usual inversion and aspiration of the upper airway with a rubber ear syringe. *Group B* includes slightly slow babies who required oxygen and a warm tub in some instances but who respired spontaneously within two minutes. *Group C* babies required more than two minutes of resuscitation before breathing spontaneously. Persistent damage was evaluated in these before discharge. *Group D* included all neonatal deaths, and *Group E* the stillborn infants. Of 307 infants, 293 or 95.4 per cent, belonged in Groups A and B. Of the eight *Group C* infants, six had definite obstetrical causes other than analgesia in the mother to explain their slow response. Since no obstetrical factor was present, it is possible that the analgesia can be implicated in the slowness of the other two babies. All eight infants were discharged in good condition. The three neonatal deaths were due to asphyxia from premature separation of the placenta, congenital malformation of the heart, and difficulty during version and extraction in an attempt to correct a transverse lie with a prolapsed arm. The three causes of death in the stillborn were erythroblastosis foetalis, asphyxia due to premature separation of the placenta with a large concealed hemorrhage, and asphyxia and intrapartum death due to a difficult breech extraction. From this analysis it is apparent that obstetrical factors other than analgesia could account for all the stillborn and neonatal deaths and for all but two of the slow *Group C* babies.

PREMATURE INFANTS

Since the depressant action of any obstetrical analgesia would be most evident among premature infants, these were studied separately. A fetal weight of less than 2,500 gm. was the criterion of prematurity. Of the 24 premature infants, 20 were classified according to their condition at delivery in Groups A and B and only four infants were in *Group C*. However, obstetrical factors other than analgesia were found to account for the slowness of respiration in all four infants. It would appear that Demerol-scopolamine analgesia has no more effect in premature infants than in those of normal weight.

CAESAREAN SECTION

Fourteen patients, delivered by caesarean section, were given 100 mg. of Demerol and 0.48 mg. (1/150 gr.) of scopolamine about an hour prior to induction of general or local anesthesia. Four operations were performed under local and

ten under general anesthesia with nitrous oxide and ether. Induction of general anesthesia proceeded quite smoothly in these patients and mucus in the respiratory passages was conspicuous by its absence. Sedation and amnesia were effective in patients who were operated upon under local anesthesia. The indications for caesarean section were:

| | |
|---|---|
| Previous caesarean for cephalopelvic disproportion | 6 |
| Large ovarian tumor complicating pregnancy | 1 |
| Small android pelvis and large fetus..... | 1 |
| Placenta previa complicating twin pregnancy | 1 |
| Central placenta previa | 1 |
| Dystocia due to cephalopelvic disproportion with adequate trial of labor..... | 4 |

The first eight were elective procedures and the remainder operations of necessity.

There were no maternal or fetal deaths, and of the 15 infants delivered, all but two were classified as Groups A and B infants. There were adequate obstetrical reasons to explain the slowness in the remaining two babies (central placenta previa with considerable blood loss and a difficult labor of 48 hours). The absence of anoxia was striking in these babies.

SUMMARY

1. Demerol and scopolamine were used for obstetrical analgesia in 300 patients at the Sonoma County Hospital.

2. Satisfactory sedation was produced in 86 per cent of the series, as compared with 48 per cent in the control group given barbiturates, paraldehyde and scopolamine in various combinations.

3. The average length of labor was 4.2 hours shorter in the primiparas and 2.2 hours shorter in multiparas given Demerol and scopolamine, than the average labors in the control group.

4. No untoward effects of importance were observed in the mothers. Mild transitory side effects consisted of dryness of the mouth and throat, nausea, dizziness, diaphoresis, vomiting, and excitement. The latter was observed in only 4 per cent as contrasted with an incidence of over 20 per cent in control patients treated with paraldehyde and barbiturates.

5. No depressant effects were observed in 307 full term and premature infants delivered vaginally.

6. The combination of Demerol and scopolamine provided an adequate and safe preanesthetic medication in a small group of caesarean sections. The absence of fetal anoxia was striking.

CONCLUSIONS

The combination of Demerol and scopolamine, as used for obstetrical analgesia, provides satisfactory relief of pain and amnesia, is safe for both mother and child, and is uncomplicated to administer and supervise. It is the most satisfactory analgesic combination employed in labor at the Sonoma County Hospital. For these reasons, it merits a wider trial by the medical profession.

DISCUSSION BY CHARLES A. ISHAM, M.D.:

I wish first to congratulate Dr. Maximov upon his excellent presentation. This subject has been adequately covered by his paper. There are a few points that can be emphasized.

In regard to caudal anesthesia, there is no argument but that this type of medication is very excellent, but it still remains that it is of very little practical use to the average private practitioner of obstetrics. Its use is chiefly limited to isolated cases or as a "one shot type" of terminal anesthesia. It has found an excellent use in the larger institutions where constant observation by house staff can be maintained, this being obligatory with this type of medication.

I have used Demerol for the last few years and have had a chance to watch its efficacy in labor. For this discussion four hundred cases were surveyed from Mercy Hospital in San Diego. This institution has entirely private cases, and there are no clinic patients available so that these patients were delivered by a large number of obstetricians. For this reason any statistical survey was entirely without any valid conclusions due to the smallness of the number after breakdown. Demerol was administered with every type of drug. Questionnaires were sent to these patients, all receiving them within a few months of their delivery. The main question was one regarding remembrance of facts during their labor. Twenty-seven per cent of 289 replies had a total amnesia, and upon investigation of this number it was found that the Demerol was given with barbiturates and scopolamine in those patients obtaining amnesia. Over 90 per cent, however, volunteered the information that the medicine was definitely of aid in their labor.

There were no appreciable severe reactions nor side effects from the administration of Demerol. The few reactions obtained were those of nausea and vomiting and slight dizziness which soon passed off. There were no fetal deaths that could be attributed to Demerol. The cyanotic infants obtained were definitely a result of other obstetrical complications.

There seemed to be much less of an "unruly" reaction on the part of the mother when receiving Demerol than with other types of agents, such as the barbiturates alone with scopolamine or paraldehyde. In 150 personal cases there were only seven "unruly" reactions, or an incidence of approximately 4 per cent.

We have found that the administration of second in 0.1 gm. or 0.2 gm. (1½ or 3 gr.) dosages and scopolamine with the first dosage of Demerol has a quieting effect and gives a very satisfactory amnesia in a large majority of cases.

DR. MAXIMOV (CLOSING)

I am aware that many writers proposing new analgesics for parturition are inclined to be enthusiastic about their particular agent. It is possible that this report has the same human failing. I would like to stress, however, that I am not advocating the use of Demerol and scopolamine to the exclusion of many other excellent anal-

gesics in common use today. Nevertheless, I am convinced that Demerol can be successfully employed in conjunction with other analgesics, or in their place, if contraindications to the other methods are present.

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Treatment of Thrombo-Embolism† By Vein Interruption

LEON GOLDMAN, M.D. and
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HOMANS¹ has called attention to "bland thrombosis" of the leg veins as a common cause of pulmonary embolism. He advocated vein ligation for the prevention of embolism after the thrombus has formed. Ochsner and DeBakey² have designated this type of vein thrombosis as "phlebothrombosis" to differentiate it from acute thrombophlebitis, in which the vein wall is actually inflamed and the thrombus is more apt to be adherent. On the basis that the leg veins are the source of the embolus in 95 per cent of the cases, Allen³ has performed a large series of vein interruptions and by this procedure has lowered the morbidity and mortality rates of pulmonary embolism and the incidence of chronic edema. He has also practiced preoperative prophylactic vein interruption in patients who could not be ambulated early.

That thrombophlebitis with its attendant edema in many patients is a late change of phlebothrombosis seems likely. Pulmonary embolism may be the only sign of phlebothrombosis, or there may be foot, calf or thigh tenderness, positive Homan's sign, slight cyanosis, mild edema, or evidence of vasospasm. Embolism is most apt to occur during the early stage and can be prevented by vein interruption. The picture of phlegmasia alba dolens is usually associated with edema, pain, fever and leukocytosis and, while the danger of embolism is not as great, the edema is more likely to persist than when associated with phlebothrombosis.

During the 26-month period between November 1, 1943, and December 31, 1945, 71 cases of thrombo-embolism were encountered on the University of California service at the San Francisco City and County Hospital. As indicated in Table 1, 25 of these patients had ligation of the iliofemoral venous system, 30 were treated by other means than ligation, and 16 of the cases were not diagnosed until autopsy and were not treated. The sex distribution was practically

equal, there being 35 males and 36 females. The ages ranged from 21 to 83, the average age being 54. Forty-six per cent occurred in the sixth decade, which again emphasizes the fact that advanced age, with its infirmities, is a predisposing factor to thrombo-embolism.

TABLE 1.—71 Cases Thrombo-embolism at S.F.H. Nov. 1, 1943 to Dec. 31, 1945

| | |
|-----------------------------------|-------|
| Ligated | 25 |
| Nonligated | 30 |
| Thrombo-embolism at autopsy | 16 |
| Total | 71 |
| Male | 35 |
| Female | 36 |
| Age | 21-83 |
| Average age | 54 |

Forty-three, or 60.6 per cent, of the 71 cases appeared on the medical service and 28, or 39.4 per cent, on the surgical service, as shown in Table 2. Of the 25 ligated cases, 13 were from the medical service and 12 from the surgical service.

TABLE 2.—Distribution of 71 Cases Thrombo-embolism S.F.H. Nov. 1, 1943 to Dec. 31, 1945

| | Medical Service | Surgical Service |
|------------------------|-----------------|------------------|
| Ligated cases | 13 | 12 |
| Nonligated cases | 18 | 12 |
| Autopsy cases | 12 | 4 |
| Total | 43 or 60.6% | 28 or 39.4% |

Thrombo-embolism occurred postoperatively in 11 of the cases in this series, as shown in Table 3. In Table 4 is seen a list of the primary diagnoses in these 71 cases of thrombo-embolism. A review of these will emphasize the variety of illnesses that may be complicated by thrombo-embolism. As has been repeatedly pointed out, cardiovascular disorders rank high as predisposing factors in

TABLE 3.—Postoperative Cases in 71 Cases Thrombo-embolism S.F.H. Nov. 1, 1943 to Dec. 31, 1945

| | |
|--|----|
| Gastric resection | 2 |
| Appendectomy | 1 |
| Oophorectomy | 1 |
| Cecostomy | 1 |
| Hernioplasty | 1 |
| Cesarean section | 1 |
| Abdominoperineal resection | 1 |
| Removal placenta | 1 |
| Drainage intra-abdominal abscess | 1 |
| Excision sarcoma leg | 1 |
| Total | 11 |

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† Read before the Section on General Medicine, Seventy-fifth Annual Session of the California Medical Association, Los Angeles, May 7-10, 1946.